Breast Cancer Survival Among American Indian and Non-Hispanic White Women
in Montana, 1980 - 2004

The incidence rate of breast cancer among American Indian women nationwide is half that of non-Hispanic White women, although incidence rates among American Indian women vary three-fold across the country.[1,2] In Montana, the age-adjusted breast cancer incidence rate for American Indian women was 121.1 per 100,000 (95% Confidence Interval 99.9 - 142.3) in 2003-2007, not statistically significantly different than the incidence rate of 120.2 per 100,000 (95% CI 115.9 - 124.5) for non-Hispanic White women.[3]

Although American Indian women have a lower incidence rate of breast cancer than non-Hispanic White women nationwide, in the past they have had a higher mortality rate, generally attributed to lower participation in screening, less insurance coverage, delay in initiating treatment, and less access to state-of-the-art treatment.[2,4,5] However, in some parts of the country, breast cancer survival has improved greatly among American Indian women and is no longer different from survival among non-Hispanic White women.[6] In Montana, the age-adjusted mortality rates from breast cancer were nearly the same: 22.1 per 100,000 (95% CI 12.1 - 32.2) for American Indian women and 21.3 per 100,000 (95% CI 19.6 - 23.0) for non-Hispanic White women in 2003-2007.[3]

The Montana Central Tumor Registry (MCTR) compared survival after diagnosis with breast cancer for American Indian and non-Hispanic White women in Montana, controlling for factors known or suspected to contribute to survival. A total of 493 American Indian and 13,964 non-Hispanic White women were identified in the MCTR. The MCTR consistently has 98% or greater ascertainment of all cases of cancer among Montana residents. In addition, Montana (along with 45 other states) collaborates with the Indian Health Service (IHS) to verify American Indian race ascertainment. Each year the MCTR reclassifies between 25 and 30 cancer patients from some other race to American Indian by this process. There are slightly more than 200 cases of cancer diagnosed among American Indian residents of Montana each year, including an average of 30 cases of breast cancer. The impact of data linkage with the IHS is therefore substantial and greatly improves the accuracy of cancer data for American Indian residents of Montana.

Women were excluded from analysis if they were lost to follow-up within five years of diagnosis, if they had benign breast disease, inflammatory breast disease, Paget's disease, lymphoma of the breast tissue, bilateral disease, multiple primary cancers, or if the breast cancer was not their first cancer (Table 1). Some women also had missing data for variables included in the analysis. The final sample consisted of 268 American Indian and 6,196 non-Hispanic White women. Half the women excluded on the basis of missing data were diagnosed in the intervals 1980-84 and 1985-89; many exclusions were due to missing data on grade/differentiation of tumors in these time periods.

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[1] CL Wiggins et al., 2008, *Cancer* 113(suppl 5):1142-1152
[2] PA Wingo et al.,2008, *Cancer* 113(suppl 5):1191-1202
[3] Montana Central Tumor Registry
[4] CB Steele et al., 2008, *Cancer* 113(suppl 5):1131-1141
[5] CI Li et al., 2003 *Arch Intern Med* 163:49-56
[6] FD Gilliland et al., 1998, *Cancer* 82:176901783; D Espy et al., 2005, *Cancer* 103:1045-1053

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Table 1. Montana Women Diagnosed with Breast Cancer, 1980 - 2004	American Indian	Non-Hispanic White
Total women indentified	493	13,964
Exclusions*		
Lost to follow-up within five years	0	27
Autopsy or death certificate only	5	118
Benign breast disease	0	1
Inflammatory breast disease	8	112
Paget's disease	5	73
Lymphoma of the breast tissue	0	10
Bilateral disease	11	285
Second or subsequent cancer diagnosis	57	1,901
Missing data**		
Grade	168	6,247
Stage	29	781
Type of surgery	2	169
No surgery	35	938
Total sample available for analysis	268	6,196

  *Some women were excluded on the basis of more than one criterion.
  ** Some women had missing data for more than one variable.

Differences before and after exclusions for missing data were statistically significant among American Indian women only for year of diagnosis and proportion of women having hormone therapy (Table 2). Differences before and after exclusions were statistically significant among non-Hispanic White women for year of diagnosis, age at diagnosis, stage at diagnosis, type of surgery, proportion of women having radiation, chemotherapy and hormone therapy, and survivorship.

Differences by race before and after exclusions were consistent for age at diagnosis, grade and stage of tumor, and the proportion for women having chemotherapy. American Indian women in the analysis were younger at diagnosis, had a higher proportion of poorly differentiated or undifferentiated tumors, a higher proportion of tumors diagnosed at the regional or distant stages, a lower proportion of breast conserving surgery, and a higher proportion of women having chemotherapy than non-Hispanic White women in the analysis. *The proportion of women who survived five or more years after diagnosis did not differ by race before or after exclusions.*

Although many women were excluded from the analysis because of missing data, the pattern of differences between American Indian and non-Hispanic White women was consistent before and after exclusions, so the exclusions should not bias the analysis. Even with the reduced sample, the analysis has adequate statistical power to detect a difference in survival between American Indian and non-Hispanic White women, should such a difference exist.

Table 2. Characteristics of Women Diagnosed with Breast Cancer by Race, Before and After Exclusions.	American Indian		Non-Hispanic White		
	Before	After	Before	After	X^2 p
Number of women	409	268	11,616	6,196	
Year of diagnosis, %					1,2
1980-84	10.0	3.4	11.2	3.1	
1985-89	12.0	3.0	16.3	5.5	
1990-94	21.3	19.0	20.5	15.6	
1995-99	24.9	33.2	25.0	34.9	
2000-04	31.8	41.2	26.9	40.9	
Age group at diagnosis, %					2,3,4
< 40 years	9.5	9.7	5.2	5.1	
40-59 years	48.9	51.5	38.6	42.2	
> 60 years	41.6	39.2	56.2	52.7	
Tumor grade, %					3,4
Well or moderately differentiated	36.4	52.6	34.8	62.9	
Poorly or not differentiated	32.0	47.4	21.3	37.1	
Missing	31.5	~	43.9	~	
Stage at diagnosis, %					2,3,4
In situ	9.8	9.3	11.5	10.8	
Local	48.2	49.3	52.9	57.3	
Regional	39.0	38.1	27.8	30.1	
Distant	5.4	3.4	3.6	1.8	
Not staged or missing	2.7	~	4.2	~	
Type of surgery, %					2,4
Breast conserving	25.9	32.5	31.5	41.4	
Mastectomy	68.5	67.5	61.8	58.6	
Surgery, not specified	5.1	~	5.3	~	
No surgery	0.5	~	1.4	~	
Had radiation, %	32.5	38.8	32.9	43.4	2
Had chemotherapy, %	38.4	45.5	26.5	33.7	2,3,4
Had hormone therapy, %	35.7	43.7	32.1	41.2	1,2
Survived five or more years, %	76.5	79.5	79.9	83.5	2

1. American Indian women significantly different before and after exclusions, p < 0.01.
2. Non-Hispanic White women significantly different before and after exclusions, p < 0.01.
3. American Indian and non-Hispanic White women significantly different before exclusions, p <0 .01.
4. American Indian and non-Hispanic White women significantly different after exclusions, p < 0.01.

All factors included in the analysis except race and having chemotherapy were statistically significantly associated with surviving five or more years after diagnosis in univariate analysis (Table 3). Overall, 83% of women survived for five or more years. The proportion surviving increased substantially with year of diagnosis, from only 63% in the interval 1980-84 to 87% in 2000-04. Only 28% of women diagnosed at the distant stage survived for five or more years, compared to 87% and 95% of women diagnosed at the local and in situ stages, respectively. Tumor grade, type of surgery, radiation therapy,

Table 3. Factors Associated with Survival for Five or More Years After Diagnosis with Breast Cancer			
	Survival		
Number of women	1,078	5,386	
	< 5 years, %	$\geq$ 5 years, %	X^2 p
Year of diagnosis			<0.0001
1980-84	36.7	63.3	
1985-89	30.8	69.2	
1990-94	20.8	79.2	
1995-99	15.5	84.5	
2000-04	12.7	87.3	
Age group at diagnosis			< 0.0001
< 40 years	17.5	82.5	
40-59 years	10.4	89.6	
$\geq$ 60 years	21.7	78.3	
Stage			<0 .0001
In situ	5.5	94.5	
Local	12.7	87.3	
Regional	24.8	75.2	
Distant	72.0	28.0	
Grade			<0 .0001
Well or moderately differentiated	12.9	87.1	
Poorly or not differentiated	23.1	76.9	
Surgery			< 0.0001
Breast conserving	11.3	88.7	
Mastectomy	20.5	79.5	
Had radiation			<0 .0001
Yes	11.0	89.0	
No	21.0	79.0	
Had chemotherapy			0.99
Yes	16.6	83.4	
No	16.7	83.3	
Had hormone therapy			< 0.0001
Yes	13.2	86.8	
No	19.2	80.8	
Race			0.09
American Indian	20.5	79.5	
Non-Hispanic White	16.5	83.5	

and hormone therapy were each associated with moderate but statistically significant differences in survival. *In spite of differences between American Indian and non-Hispanic White women in stage at diagnosis and tumor differentiation (Table 2), survival did not differ by race.*

Because many of the variables considered in this analysis are not independent in their effects on cancer survival, they were examined in a multivariate logistic regression model (Table 4). All variables that were significantly associated with survival, or for which American Indian and non-Hispanic White

Table 4. Multiple Logistic Regression Analysis of Risk of Dying within Five Years of Diagnosis				
		95% Confidence Intervals		Class comparison
Effect	Odds Ratio	Lower	Upper	Wald p
Year of diagnosis				
1980-84	1.73	1.22	2.45	< 0.05
1985-89	1.42	1.06	1.89	0.41
1990-94	1.29	1.04	1.58	0.92
1995-99	1.16	0.97	1.38	0.11
2000-04	Reference			~
Age at diagnosis				
< 40 years	0.56	0.40	0.78	0.51
50-59 years	0.39	0.33	0.46	<0 .0001
> 60 years	Reference			~
Stage				
In situ	Reference			~
Local	2.82	1.98	4.02	< 0.05
Regional	7.50	5.17	10.90	< 0.0001
Distant	65.92	37.58	115.62	< 0.0001
Grade				
Well or moderately differentiated	Reference			~
Poorly or not differentiated	1.92	1.67	2.26	< 0.0001
Surgery				
Breast conserving	0.88	0.73	1.07	0.21
Mastectomy	Reference			~
Had radiation				
Yes	Reference			~
No	1.79	1.47	2.18	<0 .0001
Had chemotherapy				
Yes	Reference			~
No	1.74	1.61	1.89	< 0.01
Had hormone therapy				
Yes	Reference			~
No	1.50	1.28	1.76	< 0.0001
Race				
American Indian	1.24	0.88	1.73	0.22
Non-Hispanic White	Reference			~

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women differed significantly, were included in the logistic model. The Odds Ratio estimates the effect of each variable on the probability of dying within five years of diagnosis while controlling for the simultaneous effects of all other variables in the model. For each variable, one level is designated as the Reference category, to which the other levels of that variable are compared. The Reference category is generally the one with the lowest risk of death within five years of diagnosis.

The effect of stage at diagnosis was especially dramatic. All other factors held constant, *women diagnosed at the distant stage were nearly 69 times more likely to die within five years of diagnosis* than women diagnosed with cancer in situ. Women diagnosed at the regional stage were seven and a half times more likely and women at the local stage were nearly three times more likely to die within five years than women diagnosed with cancer in situ. This underscores the importance of screening and early detection as the primary tool to increase breast cancer survival.

We were not able to test several hypotheses posited by other investigators for the presumed disparity in survival after breast cancer diagnosis between American Indian and non-Hispanic White women, including effects of distance to screening, diagnostic, or treatment facilities; delay in obtaining definitive diagnosis or treatment after an abnormal screening results; delay in initiating treatment; and lack of access to appropriate standard-of-care treatment.[2,4,5,7] Data to test these hypotheses are not consistently available in the MCTR. Two thirds of American Indian women and one third of non-Hispanic White women had only a post office box or other addresses that did not reflect the location of their residence so it was impossible to compute the distance to screening, diagnostic, or treatment facilities. The date of diagnosis recorded in the MCTR is the date a pathology specimen is received in the laboratory, usually a surgical specimen, so the date of diagnosis and date of initiation of treatment are effectively the same for most patients with breast cancer. The MCTR does not systematically collect information on the dates and results of mammograms. Finally, decisions about treatment for breast cancer are based on many details of an individual's case and medical history, in consultation between care providers, a woman, and perhaps her family, and cannot be adequately addressed using data available in a tumor registry.

There are no differences between American Indian and non-Hispanic White women in Montana in survival after diagnosis with breast cancer. Access to screening, diagnosis, and treatment have improved for American Indian women in Montana, as they have for White women, and barriers such as distance and lack of insurance are common to many of our residents in this largely rural and frontier state. However, it should be noted that Montana's breast cancer mortality rates among both American Indian and White women compare favorably with the national rate of 25.0 per 100,000 women.

[7] SS Gorin et al. 2006. *Arch Intern Med* 166:2244-2252.